

Effectiveness of myAirCoach: A mHealth Self-Management System in Asthma



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What is already known about this topic? The use of eHealth/mHealth in asthma care is upcoming. Many different apps and systems are currently available; however, most systems are not evaluated in a scientific setting.

What does this article add to our knowledge? This study shows that mHealth has the potential to positively influence asthma-related outcomes. Patients are also satisfied using mHealth.

How does this study impact current management guidelines? mHealth has the potential to transform health care delivery and should therefore be included as an effective option in future guidelines to support self-management.

BACKGROUND: Self-management programs have beneficial effects on asthma control, but their implementation in clinical practice is poor. Mobile health (mHealth) could play an important role in enhancing self-management.

OBJECTIVE: To assess the clinical effectiveness and technology acceptance of myAirCoach-supported self-management on top of usual care in patients with asthma using inhalation medication.

METHODS: Patients were recruited in 2 separate studies. The myAirCoach system consisted of an inhaler adapter, an indoor air-quality monitor, a physical activity tracker, a portable spirometer, a fraction exhaled nitric oxide device, and an app. The primary outcome was asthma control; secondary outcomes were exacerbations, quality of life, and technology acceptance. In

study 1, 30 participants were randomized to either usual care or myAirCoach support for 3 to 6 months; in study 2, 12 participants were provided with the myAirCoach system in a 3-month before-after study.

RESULTS: In study 1, asthma control improved in the intervention group compared with controls (Asthma Control Questionnaire difference, 0.70; $P = .006$). A total of 6 exacerbations occurred in the intervention group compared with 12 in the control group (hazard ratio, 0.31; $P = .06$). Asthma-related quality of life improved (mini Asthma-related Quality of Life Questionnaire difference, 0.53; $P = .04$), but forced expiratory volume in 1 second was unchanged. In study 2, asthma control improved by 0.86 compared with baseline ($P = .007$)

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Abbreviations used

ACQ- Asthma Control Questionnaire
CI- Confidence interval
EQ-5D-5L- EuroQol-5 Dimensions-5 Levels questionnaire
FeNO- Fraction exhaled nitric oxide
FEV1- Forced expiratory volume in 1 second
m-AQLQ- Mini Asthma-related Quality of Life Questionnaire
MCID- Minimal clinically important difference
MDI- Metered dose inhaler
mHealth- Mobile health
NO₂- Nitric dioxide
SO₂- Sulfur dioxide
TAQ- Technology Acceptance Questionnaire

and quality of life by 0.16 ($P = .64$). Participants reported positive attitudes toward the system.

DISCUSSION: Using the myAirCoach support system improves asthma control and quality of life, with a reduction in severe asthma exacerbations. Well-validated mHealth technologies should therefore be further studied. © 2020 The Authors. Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>). (J Allergy Clin Immunol Pract 2020;8:1972-9)

Key words: Asthma; mHealth; App; eHealth; Telemedicine; Self-management; Quality of life; Personalized care

Self-management plays an important role in treatment for asthma.¹ Effective self-management allows patients to use medication and devices correctly, acknowledge importance of lifestyle and environmental influences, recognize aggravating factors, and understand the value of self-monitoring. In addition, patients need to be able to recognize and treat worsening of symptoms and know when to seek urgent medical attention.² Therefore, asthma action plans are advised to support patients in evaluating and managing their symptoms.¹

However, patient adherence to self-management programs is low, with only 20% of people reporting the use of an action plan.³ Self-management tasks are often regarded as burdensome and time consuming, whereas patients indicated that they would prefer different data to be added to their asthma action plan.⁴ Current action plans based solely on symptoms and/or lung function parameters also lack precision in detecting deteriorations in asthma control and asthma exacerbations.⁵ Preferably automatically collected data could improve both precision and acceptance.

Mobile health (mHealth) support has the potential to transform health care delivery.⁶ Home-monitoring applications involving mobile device-based interactive systems are promising tools for overcoming the above-mentioned barriers and supporting self-management of asthma.⁷ mHealth can now integrate physiological, behavioral, and environmental information to aid self-management. Therefore, mHealth could encourage patients to be more engaged in self-management activities, given the ease of use of their own mobile phone.

There are over 500 mobile phone applications (apps) for asthma,⁸ but scientific evidence supporting the majority of these apps is lacking and their quality varies greatly.^{8,9} Development

and promotion of such apps presently does not appear to require evidence that they indeed improve asthma outcomes,¹⁰ which makes it difficult for patients and health care to choose the correct and effective apps for their own use.¹¹ Huckvale et al¹² reported in 2015 that 13% of the available asthma apps made recommendations about self-care procedures that were not based on scientific evidence. Importantly, non-evidence-based apps used as medical tools are potentially harmful.¹³

Therefore, the objective of the myAirCoach project was to create a validated app that would contain elements deemed necessary by patients to aid self-management.¹⁴ We have previously reported on patients' views on the required content of an asthma-related mHealth system⁴ and assessed the feasibility and end-user experience of physiological and behavioral data collection, using already available mHealth and home-monitoring tools.¹⁵

Data from these studies were used by the myAirCoach consortium (www.myaircoach.eu) to develop a mHealth system, which included an app and several portable devices, to integrate support for important self-management aspects and tasks. The system presented data to the participant on factors, including asthma control, inhalation technique, and environment exposure, thus providing patients with a wider insight into their condition and how it is affected by their environment and behavior.

In this study, we assessed the clinical effectiveness of the mHealth-supported myAirCoach self-management system in patients with asthma compared with usual care and present the results of 2 linked and simultaneously performed studies.

METHODS

Setting and participants

The myAirCoach project was EU Horizon2020 funded and conducted by a research consortium of 12 collaborating partners (list of partners available at www.myaircoach.eu). Study 1, a pragmatic randomized controlled trial, registered at www.trialregister.nl (NTR 7200), was originally planned to be performed in the Netherlands and 2 sites in the United Kingdom (UK). The study was approved by the Medical Ethics Committee of Leiden University Medical Center and North West – Greater Manchester South Research Ethics Committee.

The original sample size calculated was based on the Asthma Control Questionnaire (ACQ). To detect a difference of 0.5 (standard deviation, 0.8) points with an alpha error of 0.05 and a power of 80%, the minimum sample size needed was 41 subjects per group, 82 in total. Because of delays in obtaining ethical and Medicines and Healthcare products Regulatory Agency approval in the UK, the UK part of the study was changed to a before-after study (study 2).

Participants in both studies were eligible if they had a clinical diagnosis of asthma; were treated with controller medication with a metered dose inhaler (MDI) (Global Initiative for Asthma treatment steps 2-5¹); had a current status of asthma with an ACQ score of ≥ 1.5 ,¹⁶ and/or ≥ 1 exacerbations or hospital visits due to asthma in the previous year; were 18 years or older; and were able to understand Dutch or English in the respective countries. All participants provided written informed consent.

Design overview

Study 1 was a pragmatic randomized controlled trial in the Netherlands. Participants were included over a period of 4 months,

whereas we used a fixed end date for all participants, resulting in a varied follow-up duration (3-6 months). Participants were randomized by a computerized algorithm to receive either “usual care” or “usual care + self-management support via myAirCoach.” Study 2 was a 3-month before-after study in the UK in which all participants used the myAirCoach system.

All participants attended the research facility twice: once for a 30-minute introductory meeting and again at the end of the study. During these visits, participants completed questionnaires, and lung function (forced expiratory volume in 1 second [FEV₁]) and fraction exhaled nitric oxide (FeNO) were measured. Participants in the intervention group in study 1 and all participants in study 2 were given instructions on how to use the myAirCoach app and different devices for self-management support, lasting approximately 1 hour. In addition, all participants received periodical questionnaires through e-mail to assess outcome parameters (see this article’s Online Repository at www.jaci-inpractice.org). All participants continued care with their usual caregiver.

Intervention

The intervention was developed based on the outcomes of the focus group study and experiences of participants in the observational study.^{4,15} During the development phase, the research consortium had joint meetings with patient advisory forums to obtain feedback and prototype improvements were made accordingly. The final integrated system consisted of several devices and an app.

Devices

Both an inhaler adapter and an indoor air quality monitor were designed and produced by the myAirCoach study consortium. The inhaler adapter was an add-on that fitted different-sized MDIs, with or without spacer, and it connected to the myAirCoach app through Bluetooth. The inhaler adapter (see [Figure E1](#) in this article’s Online Repository at www.jaci-inpractice.org) was developed to improve the inhalation technique. It measured correct positioning of the inhaler during inhalation by an accelerometer. Feedback was provided with the use of indicator LEDs (red and green) on top of the inhaler adapter. In parallel, the inhaler adapter recorded sound for 24 seconds with the use of a built-in microphone. Sound analysis was performed on the order of actions (inhaling, actuation, and exhaling).¹⁷ Based on accelerometer results and sound analyses, an Inhaler Technique Score between 0 and 100 was calculated and provided to the participant in the myAirCoach app directly after use. If the Inhaler Technique Score was less than 100%, feedback on what could be improved was provided and the participant was redirected to an in-app manual for the correct inhalation technique.

The indoor air quality monitor (see [Figure E2](#) in this article’s Online Repository at www.jaci-inpractice.org), registering nitrogen dioxide (NO₂), sulfur dioxide (SO₂), particulate matter (PM_{2.5} and PM₁₀), humidity, air pressure, and temperature, was placed in the bedroom. Data, recorded every hour, were transmitted by Bluetooth to the smartphone of the participant, and results were displayed in the myAirCoach app.

Participants could monitor their FEV₁ with a portable spirometer (nSpiire Health, PiKO-1 device; available at www.nspirehealth.com) and FeNO with a home sensor (Aerocrine, NIOX VERO device; available at www.niox.com). The results were shown on the displays of the devices, and participants were asked to manually enter results in the app.

The Fitbit Charge HR (Fitbit, Inc., Fitbit charge HR; available at <http://www.fitbit.com>) is a wearable fitness tracker, measuring steps and stairs walked, calories burned, and real-time heart rate. Participants were advised to wear the Fitbit continuously. Heart rate and steps data were shown in the myAirCoach app.

myAirCoach app

At the first visit, participants downloaded the myAirCoach app on their smartphone. Because the app was only used in a research setting and required anonymity, the app was not publicly available, but could only be downloaded with the help of the research team. Every participant was also given an anonymous username and password, and logging in was required the first time they used the app. In the app, results from all devices were displayed in graphs. In addition, participants were able to monitor symptoms with questionnaires, including the Asthma Control Diary,¹⁸ ACQ,¹⁹ and Sino-Nasal Outcome Test-22²⁰ (see [Table E2](#) in this article’s Online Repository at www.jaci-inpractice.org). Outdoor air quality, measured by the European Copernicus Program (www.regional.atmosphere.copernicus.eu), was also displayed for current location or other favorite locations. A map using color-coding to indicate levels of pollution was provided in addition to an overall statement on air pollution and concentrations of ozone, ultrafine dust, fine dust, carbon monoxide, NO₂, and SO₂. More detailed information on the app and devices is provided in this article’s Online Repository at www.jaci-inpractice.org (including [Figures E3-E7](#), available in this article’s Online Repository at www.jaci-inpractice.org).

Outcomes and follow-up

For both studies, the primary outcome was asthma control assessed by the ACQ (range, 0-6; minimal clinically important difference [MCID] = 0.5) at 4-week intervals.¹⁹ A lower score represents better asthma control.

Secondary outcomes were severe asthma exacerbation rate, quality of life, FEV₁, and technology acceptance. Severe exacerbations were defined as asthma-related hospitalizations, emergency care visits, or systemic use of oral corticosteroids for ≥ 3 days.²¹ Asthma-related quality of life was measured by the mini Asthma Quality of Life Questionnaire (m-AQLQ) (MCID = 0.5),²² consisting of 4 domains: symptoms, activities, emotions, and environment, at 12-week intervals. Generic health-related quality of life was assessed by the EuroQol-5 Dimensions-5 Levels (EQ-5D-5L) questionnaire at 12-week intervals.²³ FEV₁ was measured with the PiKO-1 device throughout the study for the intervention participants and during the visits for the controls. Participant attitudes toward and acceptance of the technology were measured by the Technology Acceptance Questionnaire (TAQ) at 12 weeks.²⁴ The TAQ has 11 domains next to specific questions about the inhaler adapter and the PiKO-1 device (see this article’s Online Repository at www.jaci-inpractice.org).

Statistical analysis

In study 1, the outcomes of the ACQ, m-AQLQ, EQ-5D-5L, and FEV₁ were analyzed using a mixed-model analysis, adjusting for repeated measurements within participants, and baseline values of the outcomes. Severe exacerbation rates were compared by the Cox proportional hazard model, allowing analysis of multiple exacerbations per participant. For study 2, paired *t*-tests were performed for the ACQ, m-AQLQ, EQ-5D-5L, and FEV₁ comparing baseline measurements with the final results. Boxplots for the TAQ were

TABLE I. Participant demographics

	Study 1 (RCT in the Netherlands)			Study 2 (before-and-after study in the UK)
	Control (n = 15)	Intervention (n = 15)	P value	(n = 12)
Age (y), mean (SD)*	49.1 (11.0)	51.3 (13.2)	.65	41.3 (13.8)
Gender, n female*	11	12	.68	10
Internet experience, n [†]			.27	
None	0	1		
A little	1	1		
Quite a lot	2	6		2
A lot	11	7		10
Smoking, n [‡]			.14	
Yes	0	0		1
No	11	7		10
Previously	4	8		1
Season enrolled, n [‡]			.66	
Winter	2	1		0
Spring	11	13		0
Summer	2	1		12
GINA medication step, n [‡]			.25	
2	0	3		1
3	8	6		2
4	0	1		1
5	2	2		
Severe exacerbations previous year, n [‡]	13	14	.54	8
Age at diagnosis (y), mean (SD)*	26.1 (18.6)	19.5 (21.1)	.39	16.4 (18.4)
FEV1 (L), median (IQR) [‡]	2.3 (1.4-2.9)	2.1 (1.5-3.0)	.85	2.5 (1.9-3.4)
FeNO (parts per billion), median (IQR) [‡]	18 (13-28)	14 (12-22)	.45	17 (11.5-54)
ACQ, mean (SD) score*	2.31 (0.97)	2.33 (0.78)	.94	1.59 (0.88)
Controlled (n)	0	0		3
Partly controlled (n)	3	3		3
Uncontrolled (n)	11	11		6
SNOT22, mean (SD) score*	35.9 (18.4)	40.4 (17.9)	.52	27.9 (12.0)

ACQ, Asthma Control Questionnaire; FeNO, fraction exhaled nitric oxide; FEV1, forced expiratory volume in 1 second; GINA, Global Initiative for Asthma; IQR, interquartile range; RCT, Randomized Control Trial; SD, standard deviation; SNOT-22, Sino-Nasal Outcome Test-22.

*Calculated with *t*-test.

†Calculated with χ^2 .

‡Mann-Whitney *U* test.

made, combining results of all participants using the system in both study 1 and 2. All analyses were performed with STATA 14.0 (StataCorp, College Station, Tex).

RESULTS

Subjects

Thirty participants were included in study 1, and 12 participants in study 2 (see Figure E8 in this article's Online Repository at www.jaci-inpractice.org). The major reason for declining participation was concern about time. Two participants dropped out of study 1: 1 in the intervention group due to "personal circumstances" and 1 control (no further response to repeated enquiry). The mean follow-up in the intervention group was 166 days and in the control group 154 days. All participants from study 2 finished follow-up with a mean follow-up of 94 days.

Baseline characteristics are shown in Table I. There were no significant differences between control and intervention groups in study 1. Participants in study 2 had a slightly different profile than participants of study 1. They were on average 10 years

younger, their age of diagnosis was also lower, FeNO was higher, and their baseline ACQ was better.

System use

The app was used for 2345 tasks. These tasks included filling out questionnaires and entering FeNO/FEV1 data (see Table E1 in this article's Online Repository at www.jaci-inpractice.org). In study 1, on average, 110 tasks per patient were performed, and in study 2, this was on average 67 times.

The number of inhalations registered by the system in study 1 was 219 per patient, and in study 2, this was 81 per patient. In study 1, the Inhaler Technique Score changed by 1% (from 79% to 80%). In study 2, the Inhaler Technique Score changed from 88% to 76%.

Outcomes

The intervention group had a clinically relevant and statistically significant improvement of asthma control compared with the control group in study 1. In the mixed-model analysis, the difference in ACQ was 0.70 (95% confidence interval [CI], -1.21; -0.20; *P* = .006) (Table II). A sensitivity

TABLE II. Outcome measures

	Study 1		Study 2	
	Difference intervention-control	P value	Difference exit-baseline	P value
ACQ, score	-0.70	.006	-0.86	.007
m-AQLQ, score	0.53	.04	0.16	.64
EQ-5D-5L, score	0.12	.04	0.04	.23
FEV1 (L)	-0.09	.60	-0.11	.42

Differences as assessed by mixed-model analysis, adjusting for repeated measurements within participants, and baseline values of the outcomes.

ACQ, Asthma Control Questionnaire; EQ-5D-5L, EuroQol-5 Dimensions-5 Levels questionnaire; FEV1, forced expiratory volume in 1 second; m-AQLQ, mini Asthma-related Quality of Life Questionnaire.

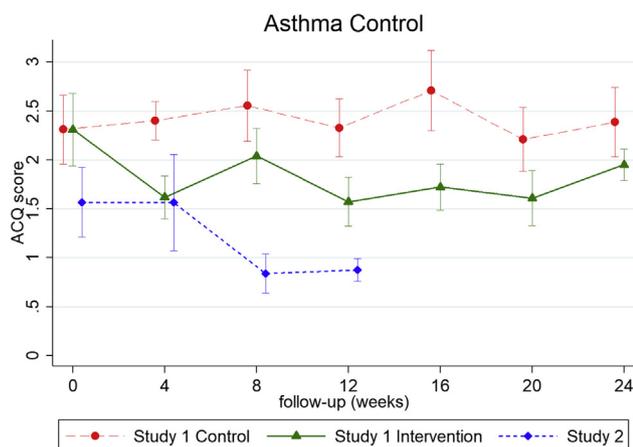


FIGURE 1. Asthma Control Questionnaire (ACQ). Asthma control measured by ACQ. Lower score represents better asthma control (minimal clinically important difference = 0.5). Note: not all participants finished 6-month follow-up because of a fixed end date; mean follow-up was 149 days (5 months) in study 1. A questionnaire filled in within 14 days of enrollment is regarded as baseline. In study 1, 28 of 30 participants finished 12-week follow-up and 5 participants (17%) had more than 24-week follow-up. Error bars represent 95% confidence interval. Points in the graph have been shifted slightly to the left or the right to avoid overlap of error bars.

analysis additionally adjusting for baseline characteristics age, smoking status, age of diagnosis, and gender and a sensitivity analysis for baseline FEV1 and FeNO showed similar results. In study 2, asthma control improved by 0.86 (95% CI, 0.29; 1.44; $P = .007$) compared with baseline, as shown in Figure 1.

The number of severe exacerbations was lower in the intervention group compared with the control group for study 1 (respectively, 6 vs 12 [hazard ratio, 0.31; 95% CI, 0.09; 1.06; $P = .06$], see Figure 2). Exacerbation rate for intervention participants was 0.94 per participant per year, compared with 2.04 per participant per year for the participants in the control group. In study 2, 3 exacerbations occurred. Exacerbation rate was 1.06 per participant per year.

The difference in m-AQLQ assessed by the mixed-model analysis was 0.53 (95% CI, -0.22; 1.10; $P = .04$) (Figure 3). The differences in the subdomains “symptoms” and “emotions” both exceeded the MCID of 0.5 and were statistically significant (Table E3 and Figure E9, available in this article’s Online Repository at www.jaci-inpractice.org). In study 2, the participants

had a baseline m-AQLQ of 5.13, and their score increased by 0.16 ($P = .64$). The participants improved in all domains, with the largest improvement in the “emotions” domain.

The EQ-5D-5L showed an improvement in generic health-related quality of life in the intervention group (coefficient, 0.12; $P = .04$) in study 1 compared with the controls. In study 2, there was no significant difference in EQ-5D-5L score between baseline and exit (0.04; $P = .23$), as shown in Figure E10 (available in this article’s Online Repository at www.jaci-inpractice.org).

There was no change in FEV1 measured in both studies. In study 1, the FEV1 was 0.09 L ($P = .60$) lower in the intervention group compared with the control group (see Figure E11 in this article’s Online Repository at www.jaci-inpractice.org). In study 2, participants had a baseline FEV1 of 2.63 L and their exit FEV1 was 2.52 L ($P = .42$).

The TAQ showed favorable attitudes of the participants toward the myAirCoach intervention except for the impact of the system on social influence and attitude toward the inhaler adapter. Participants were most positive on the facilitating conditions and trust in the system. They also reported favorable attitudes on the self-management aspect of the system. The average domain scores are depicted in Figure 4.

DISCUSSION

Our study shows that mHealth-supported self-management aided by the myAirCoach system was effective in clinically improving asthma control, exacerbation rates, and quality of life. In addition, end-users of this mHealth platform reported generally positive attitudes toward the system.

In asthma, most research in eHealth has focused on using traditional forms of telemedicine, including remote consultations and SMS reminders.²⁵⁻²⁷ Even though Huckvale et al¹² already reported 764 different asthma apps in 2015, the number of trials focusing on mobile app-assisted self-management in asthma is limited.²⁸ Moreover, none of the apps assessed in previous studies additionally used such diverse data from wearables, environmental databases, and home-monitoring devices.²⁹ As a consequence of our multifaceted intervention, we opted to assess clinical outcomes, such as asthma control and exacerbation rate. Other studies have focused more on outcomes particularly relevant for medication adherence. For example, the recent ADAPT study by Kosse et al³⁰ developed an app with several modules primarily targeting adherence in adolescents, and they showed that their app indeed improved this.

A Cochrane review in 2012 (updated in 2013) included only 2 studies regarding asthma self-management with apps compared with paper-based asthma self-management.³¹ Ryan et al³²

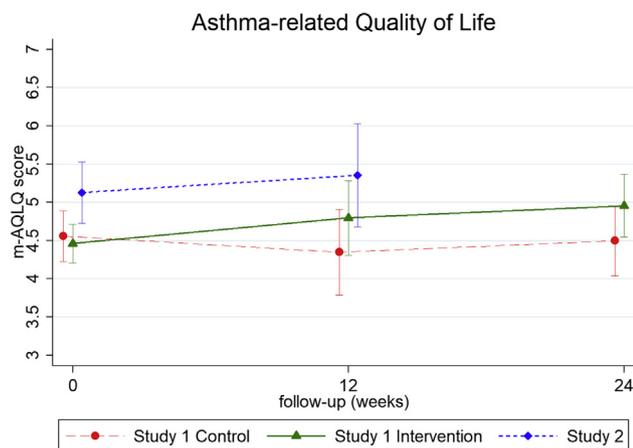


FIGURE 2. Time until first exacerbation per participant. Proportion exacerbation plotted against follow-up time. The numbers depicted in the graph indicate the participants still in follow-up. *m-AQLQ*, Mini Asthma-related Quality of Life Questionnaire.

concluded that monitoring of asthma through mobile phone use does not improve asthma outcomes more than paper-based strategies. Both groups showed clinically relevant improvements in asthma control and quality of life. It is suggested that monitoring in itself could have a positive effect on asthma-related outcomes. However, paper monitoring could be more cumbersome and time consuming for the participant, and it does not allow for collection of other types of data, such as heart rate. mHealth is more user-friendly because a majority of the adults use a smartphone.³³

A study by Cook et al³⁴ was a promising proof of concept study showing the effectiveness of an asthma-related mHealth application. The asthma-related outcomes (asthma control and FEV1) improved, and patients were satisfied with the intervention. This study however only consisted of an intervention group without randomization. Our study supports and extends these findings because we have found a beneficial effect on asthma control, severe asthma exacerbations, and quality of life and we included a control group in the first study to minimize the effect of confounding factors unrelated to the mHealth. We also reported a high user-satisfaction.

An important aspect of the myAirCoach project was the involvement of participants in different stages of the development of our intervention, including repeated device testing to improve performance. We specifically asked what kind of functionalities they wanted to see in a mHealth system and what they deemed useful information. If no device existed that could measure these parameters, we developed it within our study consortium. Overall, the participants were satisfied with the system and they reported that they felt the system aided them in their self-management. We believe that this early involvement of patient users in this project has helped in devising a user-friendly tool for self-management of asthma.

An important strength of our study is that we provided participants with an app that included a wide variety of data on very different aspects of asthma management. The app was used often, with 110 tasks per patients on average in study 1 and 67 tasks per patient in study 2. We were only able to record a task if the participant manually entered data into the app (answering a

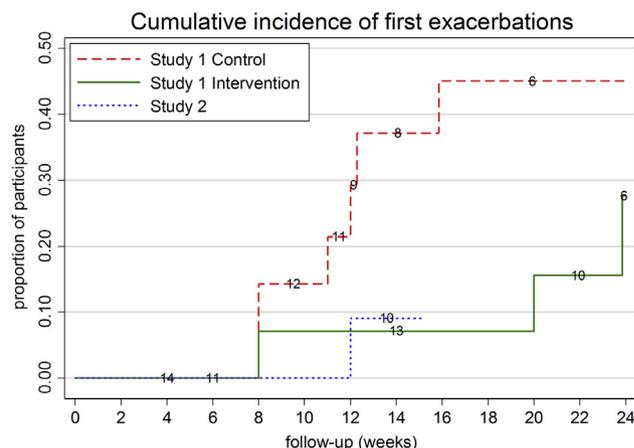


FIGURE 3. Mini Asthma Quality of Life Questionnaire (m-AQLQ). Asthma-related quality of life measured by the m-AQLQ. Higher score represents better quality of life (minimal clinically important difference = 0.5). Note: not all participant finished 6-month follow-up in study 1. Error bars represent 95% confidence interval. Points in the graph have been shifted slightly to the left or the right to avoid overlap of error bars.

questionnaire, entering a measurement). So, the average numbers of tasks indicate the minimal usage, because any other action in the app (eg, viewing of inhalation score, air quality data, or individual graphs on symptoms and measurements) was not recorded.

Although we showed that by providing a comprehensive overview we managed to improve asthma control, exacerbation rate, and quality of life, we do not know how much each of the individual components contributed to these improvements. This also relates to the fact that we did not record viewing of results in the app of, for example, the inhalation technique score. We know this improved in some and worsened in others. However, we do not know who actually viewed their inhalation technique results in the app, or who acted on these results, for example, by viewing the in-app inhalation instructions or by going to their health care professional. Different components are relevant for different patients. In future studies, we recommend to also systematically collect data on page views and time spent on different components of an app and preferably also on subsequent self-management changes made by patients.

An important limitation of the study is the number of participants included in the study. In the original protocol, the intention was to include 90 participants in the study (45 intervention and 45 control). Because of the fixed end date of the study appointed by the European Union, combined with strict regulatory laws regarding studies with medical devices in the UK and longer than expected development time of the app and devices, we were only able to include 30 (randomized) participants in the study site in the Netherlands. All UK participants were allocated to the use of the myAirCoach system to get as much feedback on the system as possible in a before-after study setting. Even though the number of participants included in the Randomized Controlled Trial was limited, the primary outcome parameter improved. One might argue that this might be due to overestimation of the real effect, also known as the winner's curse. However, because most secondary outcomes also

Technology Acceptance

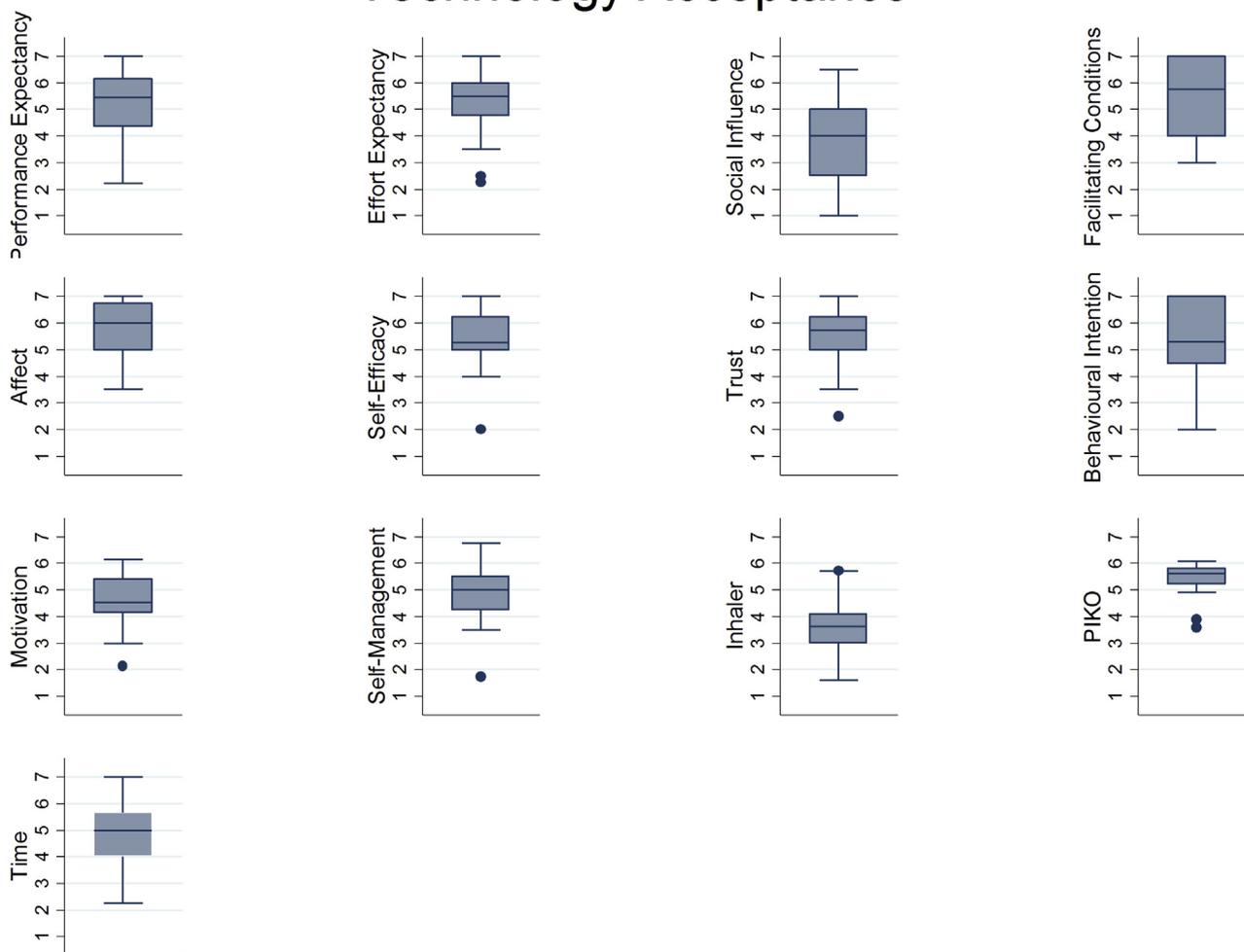


FIGURE 4. Boxplots of the Technology Acceptance Questionnaire domains. Thirteen domains of the Technology Acceptance Questionnaire tested in both studies combined. Patients reported how much they agreed with the questionnaire statements on a 7-point Likert scale (ranging from completely disagree = 1 to completely agree = 7). The higher a score, the more favorable the attitudes of the participants toward the myAirCoach system were. In the figure, all 13 domains are plotted and the scores are depicted on the y-axis of every boxplot.

showed a consistent improvement and the effect was still statistically significant after correction for multiple tests, we are confident that the myAirCoach system had a positive effect on asthma-related outcomes.

Another limitation is the lack of long-term data of the system. Participants in the Netherlands used the system for a maximum of 6 months. Even though participants reported in the TAQ that they were willing to continue using the system, it is unknown if the positive effects on asthma control would be sustained after a longer period. Another important aspect is the influence of seasonal factors on the results of our study, because we do not have a year follow-up time. Next, in 74% of the inhalation, no inhalation technique score could be calculated because of technical issues, possibly explaining the negative attitudes of the patients toward the inhaler add-on in the TAQ.

Even though the age of participants was highly variable (23-77 years), future studies are called for to further evaluate mHealth systems in larger and more diverse groups. In future projects,

predictive modeling could be used to make personalized recommendations given by the system to further enhance self-management.

CONCLUSION

We have shown a clinically significant beneficial effect of the myAirCoach mHealth intervention on asthma-related outcomes. Asthma control, quality of life, and exacerbation rate improved during the study. Overall, participants were satisfied with the myAirCoach study app and intervention.

DATA AVAILABILITY

Data analyzed in this manuscript are available on request.

REFERENCES

1. The Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention 2018. Available from: www.ginasthma.org. Accessed September 30, 2019.

2. Reddel HK, Jenkins CR, Partridge MR. Self-management support and other alternatives to reduce the burden of asthma and chronic obstructive pulmonary disease. *Int J Tuberc Lung Dis* 2014;18:1396-406.
3. Haughney J, Barnes G, Partridge M, Cleland J. The Living & Breathing Study: a study of patients' views of asthma and its treatment. *Prim Care Respir J* 2004; 13:28-35.
4. Simpson AJ, Honkoop PJ, Kennington E, Snoeck-Stroband JB, Smith I, East J, et al. Perspectives of patients and healthcare professionals on mHealth for asthma self-management. *Eur Respir J* 2017;49:1601966.
5. Honkoop PJ, Taylor DR, Smith AD, Snoeck-Stroband JB, Sont JK. Early detection of asthma exacerbations by using action points in self-management plans. *Eur Respir J* 2013;41:53-9.
6. World Health Organization. mHealth: new horizons for health through mobile technologies. Global Observatory for eHealth series; 2011. Available from: https://www.who.int/goe/publications/goe_mhealth_web.pdf. Accessed September 30, 2019.
7. Kikidis D, Konstantinos V, Tzouvaras D, Usmani OS. The digital asthma patient: the history and future of inhaler based health monitoring devices. *J Aerosol Med Pulm Drug Deliv* 2016;29:219-32.
8. Tinschert P, Jakob R, Barata F, Kramer JN, Kowatsch T. The potential of mobile apps for improving asthma self-management: a review of publicly available and well-adopted asthma apps. *JMIR Mhealth Uhealth* 2017;5:e113.
9. Wu AC. The promise of improving asthma control using mobile health. *J Allergy Clin Immunol Pract* 2016;4:738-9.
10. Apple Inc. App store review guidelines; 2008. Available from: <https://developer.apple.com/app-store/review/guidelines>. Accessed September 30, 2019.
11. Anderson K, Burford O, Emmerton L. Mobile health apps to facilitate self-care: a qualitative study of user experiences. *PLoS One* 2016;11:e0156164.
12. Huckvale K, Morrison C, Ouyang J, Ghaghda A, Car J. The evolution of mobile apps for asthma: an updated systematic assessment of content and tools. *BMC Med* 2015;13:58.
13. Buijink AW, Visser BJ, Marshall L. Medical apps for smartphones: lack of evidence undermines quality and safety. *Evid Based Med* 2013;18:90-2.
14. Kikidis D, Votis K, Tzouvaras D. MyAirCoach: designing a mobile application for the education of patients regarding asthma disease. *IEEE Interactive Mobile Communication Technologies and Learning (IMCL)*: Thessaloniki, Greece; 2015.
15. Honkoop PJ, Simpson A, Bonini M, Snoeck-Stroband JB, Meah S, Fan Chung K, et al. MyAirCoach: the use of home-monitoring and mHealth systems to predict deterioration in asthma control and the occurrence of asthma exacerbations; study protocol of an observational study. *BMJ Open* 2017;7: e013935.
16. Juniper EF, Bousquet J, Abetz L, Bateman ED, Committee GOAL. Identifying 'well-controlled' and 'not well-controlled' asthma using the Asthma Control Questionnaire. *Respir Med* 2006;100:616-21.
17. Nousias S, Lalos AS, Arvanitis G, Moustakas K, Tsirelis T, Kikidis D, et al. An mHealth system for monitoring medication adherence in obstructive respiratory diseases using content based audio classification. *IEEE Access* 2018;6: 11871-82.
18. Juniper EF, O'Byrne PM, Ferrie PJ, King DR, Roberts JN. Measuring asthma control. Clinic questionnaire or daily diary? *Am J Respir Crit Care Med* 2000; 162(Pt 1):1330-4.
19. Juniper EF, O'Byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. *Eur Respir J* 1999;14: 902-7.
20. Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 22-item Sinonasal Outcome Test. *Clin Otolaryngol* 2009;34:447-54.
21. Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J* 2014;43:343-73.
22. Juniper E. Determining a minimal important change in a disease-specific quality of life questionnaire. *J Clin Epidemiol* 1994;47:81-7.
23. EuroQol. EQ-5D-5L. Available from: <https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/2009>. Accessed September 30, 2019.
24. Wang W, van Lint CL, Brinkman WP, Rovekamp TJM, van Dijk S, van der Boog PJM, et al. Renal transplant patient acceptance of a self-management support system. *BMC Med Inform Decis Mak* 2017;17:58.
25. Ahmed S, Ernst P, Bartlett SJ, Valois MF, Zaihra T, Pare G, et al. The effectiveness of web-based asthma self-management system, My Asthma Portal (MAP): a pilot randomized controlled trial. *J Med Internet Res* 2016;18:e313.
26. van Gaalen JL, Beerthuisen T, van der Meer V, van Reisen P, Redelijkheid GW, Snoeck-Stroband JB, et al. Long-term outcomes of internet-based self-management support in adults with asthma: randomized controlled trial. *J Med Internet Res* 2013;15:e188.
27. Zhao J, Zhai YK, Zhu WJ, Sun DX. Effectiveness of telemedicine for controlling asthma symptoms: a systematic review and meta-analysis. *Telemed J E Health* 2015;21:484-92.
28. Hui CY, Walton R, McKinstry B, Jackson T, Parker R, Pinnock H. The use of mobile applications to support self-management for people with asthma: a systematic review of controlled studies to identify features associated with clinical effectiveness and adherence. *J Am Med Inform Assoc* 2017;24:619-32.
29. Katwa U, Rivera E. Asthma management in the era of smart-medicine: devices, gadgets, apps and telemedicine. *Indian J Pediatr* 2018;85:757-62.
30. Kosse RC, Bouvy ML, de Vries TW, Koster ES. Effect of a mHealth intervention on adherence in adolescents with asthma: a randomized controlled trial. *Respir Med* 2019;149:45-51.
31. Marcano Belisario JS, Huckvale K, Greenfield G, Car J, Gunn LH. Smartphone and tablet self management apps for asthma. *Cochrane Database Syst Rev* 2013;(11):CD010013.
32. Ryan D, Price D, Musgrave SD, Malhotra S, Lee AJ, Ayansina D, et al. Clinical and cost effectiveness of mobile phone supported self monitoring of asthma: multicentre randomised controlled trial. *BMJ* 2012;344:e1756.
33. Ofcom. Communications Market Report; 2018. Available from: <https://www.ofcom.org.uk/research-and-data/multi-sector-research/cmr/cmr-2018>. Accessed September 30, 2019.
34. Cook KA, Modena BD, Simon RA. Improvement in asthma control using a minimally burdensome and proactive smartphone application. *J Allergy Clin Immunol Pract* 2016;4:730-737.e1.

ONLINE REPOSITORY

Flowchart participant inclusion
Generic health-related quality of life
Lung function

DEVICES AND APP

The app could be downloaded if the participant had an android phone. If participants used Apple's iPhone, the app could not be installed on their smartphone because every iPhone is linked with a personal Apple account (Apple ID), which prevents anonymous processing of data, because all recorded data are also shared with Apple. Therefore, participants with an iPhone were given an iPod Touch with an anonymous Apple ID specifically created for this study. The iPod Touch was a sixth-generation iPod that works in a similar fashion as the iPhone these participants normally used.

When the app was opened, participants could navigate to one of the 5 menus: "Dashboard," "Measurements," "Calendar," "Messages," and "Me." The menu "Dashboard" (Figure E3) was divided into 5 tabs (at the top of the screen) of which "At a Glance" was the main screen. Here participants could see a quick summary of the most recent measurements in a general overview. In the second screen named "Action Plan," an asthma action plan was shown to the participants. In the third tab "Questionnaires," participants could fill out the Asthma Control Diary (ACD), Asthma Control Questionnaire (ACQ), or Sino-Nasal Outcome Test-22 (SNOT22) questionnaires. The tabs "Goals" and "Notifications" allowed participants and health care providers to set personalized goals (eg, amount of steps a day) and receive (update) notifications. In the screenshots below demo scores are depicted as an illustration.

The second menu at the bottom was "Measurements" (Figure E4), which was divided into 3 main categories: "Health," "Activity," and "Environmental." In "Health," participants could see an overview of their personal scores of inhaler use, fraction exhaled nitric oxide (FeNO), spirometry, and their questionnaires (ACD/ACQ, SNOT22). In "Activity," participants could see an overview of their Fitbit data. In "Environmental," participants were able to access air quality data for outdoor air quality (www.regional.atmosphere.copernicus.eu) and indoor air quality (measured by the indoor air quality monitor).

Participants could select every individual measurement to see an overview over time (see Figure E5). Mean scores were calculated and displayed in a visual manner. More detailed information about individual measurements was available by pressing the "all data" button.

In the "Calendar," participants were shown measurements in a calendar to more easily identify days with worse (or better) asthma control, as well as to have a complete overview and history of their actions. Participants could also manually enter notes about specific events to facilitate in recollecting these details when discussing their asthma with a health care professional a few months later (a feature specifically requested by participants).⁴

In the "Messages" tab, participants could chat in real time with the research team. In possible future projects, participants could use this function to chat with their own health care provider. The final tab "Me" was a settings function with guides for the app, inhalation technique instruction material, and links to

useful websites on asthma. In this tab participants could also enable or disable the virtual support "Airica" (Figure E6) that recognized voice commands and text inputs. Airica is based on artificial intelligence, such as machine learning algorithms and natural language processing concepts.

The inhaler add-on shown in Figure E1 was an add-on to normal metered dose inhalers. After activating the device by shaking it, it connected to the app. A screen would pop up and sound recording would start, which is shown in figure E7. After sound recording was finished, data were uploaded, processed, and then sent back to the app. A score was calculated varying from 0% to 100% and displayed to the participant.

The indoor air quality monitor (air quality sensor) was a black cube connected through Bluetooth with the smartphone and the app. It was roughly 7 cm × 7 cm × 7 cm (Figure E2). Data were recorded every hour, temporarily stored on an internal memory, and transmitted to the phone when available. Participants were asked to hold their smartphone at least daily within Bluetooth vicinity of the indoor air quality monitor to allow data transfer.

ACTIVITIES

Participants were asked to fill out questionnaires and do measurements frequently. Questionnaires not described in this manuscript are the Food Frequency Questionnaire (GA²LEN FFQ), Hospital Anxiety and Depression Scale (HADS), Health Education Impact Questionnaire (heiQ), Sino-Nasal Outcome Test (SNOT-22), and Cost-Q. The Asthma Control Diary (ACD) is a questionnaire comparable with the ACQ, except it asks questions about the previous day (compared with the previous week).

m-AQLQ DOMAINS

The m-AQLQ can be divided into 4 domains: symptoms, activities, emotions, and environment (Table E3; Figure E9). In study 1, improvements in "symptoms" and "emotions" were both clinically and statistically significant. Improvements in the "environments" domain also exceeded the minimal clinically important difference.

TECHNOLOGY ACCEPTANCE QUESTIONNAIRE (TAQ)

The 13 domains of the TAQ are as follows:

- (1) Performance expectancy: the degree to which participants believe that using the system will help them attain gains or make losses with the performance of their health management
- (2) Effort expectancy: the degree of ease associated with the use of the system
- (3) Social influence: the degree to which participants perceive that important others believe that they should use the system
- (4) Facilitating conditions: the degree to which participants believe that there are objective factors available in their environment to support their use of the system
- (5) Affect: participants' overall affective reaction toward using the system
- (6) Self-efficacy: the degree to which participants judge themselves capable of using the system to manage their health

- (7) Trust: the degree to which participants believe that using the system will occur in a safe and reliable manner
- (8) Behavioral intention: the degree to which an individual intends to use the myAirCoach system for managing his or her health
- (9) Motivation: the degree to which an individual is motivated to continue the myAirCoach system for managing his or her health
- (10) Self-management: participants' opinion on conducting self-management through the system
- (11) Inhaler adapter: participants' opinion on the myAirCoach inhaler adapter
- (12) PiKO-1: participants' opinion on the PiKO-1 home spirometer
- (13) Time: the degree to which an individual is satisfied with the amount of time it takes to use the system

TABLE E1. Number of times the app was used to perform tasks

	Study 1	Study 2	Total
ACD	130	177	307
ACQ	70	27	97
FeNO	570	213	783
SNOT22	67	34	101
Spirometry	700	357	1057
Total	1537	808	2345

ACD, Asthma Control Diary; ACQ, Asthma Control Questionnaire; FeNO, fraction exhaled nitric oxide; SNOT-22, Sino-Nasal Outcome Test-22.

TABLE E2. Study procedures

Frequency of tests	First visit	Intervention		Control		Final visit
		1- to 2-wk training phase	Follow-up	1-wk test phase	Follow-up	
Patient questionnaires						
ACD or ACQ	Once	Daily	Monthly	—	Monthly	Once
Current medication record	Once	Daily	Monthly	—	Monthly	Once
Exacerbations history	Once	Daily	Monthly	—	Monthly	Once
m-AQLQ	Once	—	3-monthly	—	3-monthly	Once
GA ² LEN FFQ	Once	—	—	—	—	—
HADS	Once	—	—	—	—	—
heiQ	Once	—	3 months	—	3 months	Once
SNOT-22	Once	—	Monthly	—	Monthly	Once
EQ-5D-5L	Once	—	3-monthly	—	3-monthly	Once
Cost-Q	—	—	3-monthly	—	3-monthly	Once
Technology Acceptance Questionnaire	—	—	3 months	—	—	Once
Physiological sensors						
Portable spirometry	Once	Daily	Weekly	—	—	—
FeNO	Once	Daily	Weekly	—	—	Once
Heart rate and activity level	Once	Continuous	Continuous	—	—	—
Monitors						
Inhaler usage monitoring	Once	Continuous	Continuous	—	—	—
External environmental monitoring	—	Continuous	Continuous	—	—	—

ACD, Asthma Control Diary; ACQ, Asthma Control Questionnaire; EQ-5D-5L, EuroQol-5 Dimensions-5 Levels questionnaire; FeNO, fraction exhaled nitric oxide; GA²LEN FFQ, Food Frequency Questionnaire; HADS, Hospital Anxiety and Depression Scale; heiQ, Health Education Impact Questionnaire; m-AQLQ, mini Asthma-related Quality of Life Questionnaire; SNOT-22, Sino-Nasal Outcome Test.

TABLE E3. Quality of life per domain

Domain	Study 1*		Study 2†	
	Difference	P value	Change	P value
Symptoms	0.69	.03	0.22	.51
Activities	0.32	.41	0.10	.83
Emotions	0.54	.04	0.25	.44
Environment	0.53	.08	0.03	.94

*Study 1. Randomized Control Trial: intervention compared with controls with mixed-model analysis.

†Study 2. Before-and-after study: baseline compared with end of follow-up with the paired *t*-test.

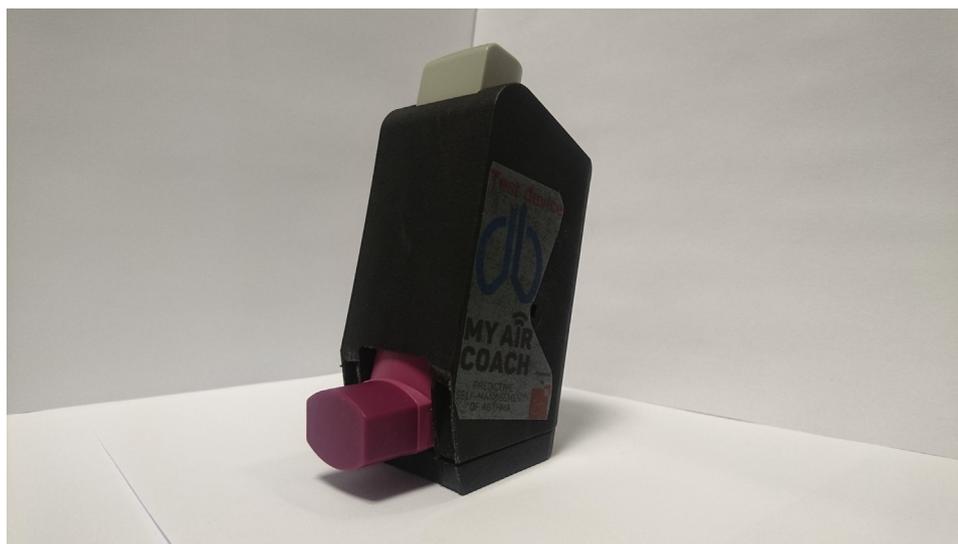


FIGURE E1. myAirCoach inhaler add-on. The inhaler add-on was capable of measuring several critical parameters, such as correct positioning of the inhaler during inhalation as well as the sound of the inhalation procedure.



FIGURE E2. myAirCoach air quality monitor. The indoor air quality monitor is capable of measuring several indoor parameters such as nitrogen dioxide (NO₂), sulfur dioxide (SO₂), particulate matter (PM2.5 and PM10), humidity, air pressure, and temperature.

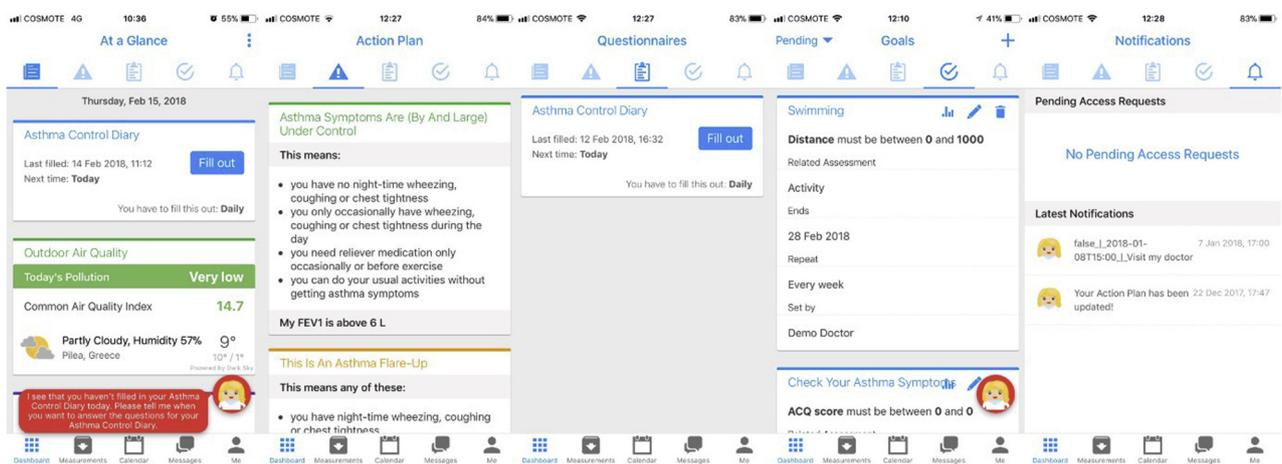


FIGURE E3. myAirCoach app: Dashboard. Different aspects of the myAirCoach app: “At a Glance,” “Action Plan,” “Questionnaires,” “Goals,” and “Notifications.”

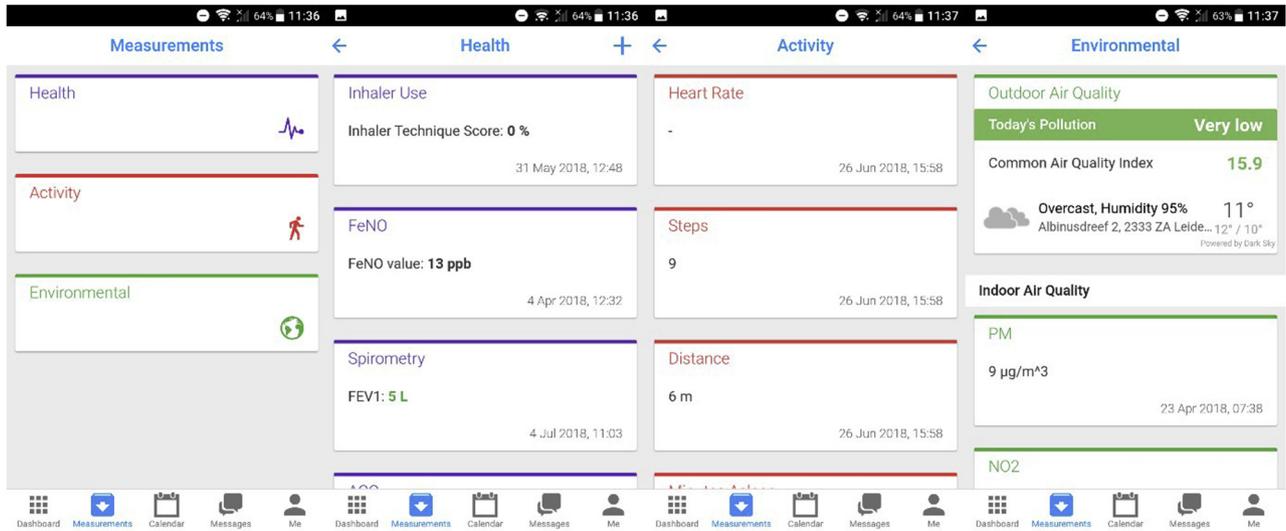


FIGURE E4. myAirCoach app: Measurements. Various categories of measurements are presented to the participant: “Health,” “Activity,” and “Environmental.”

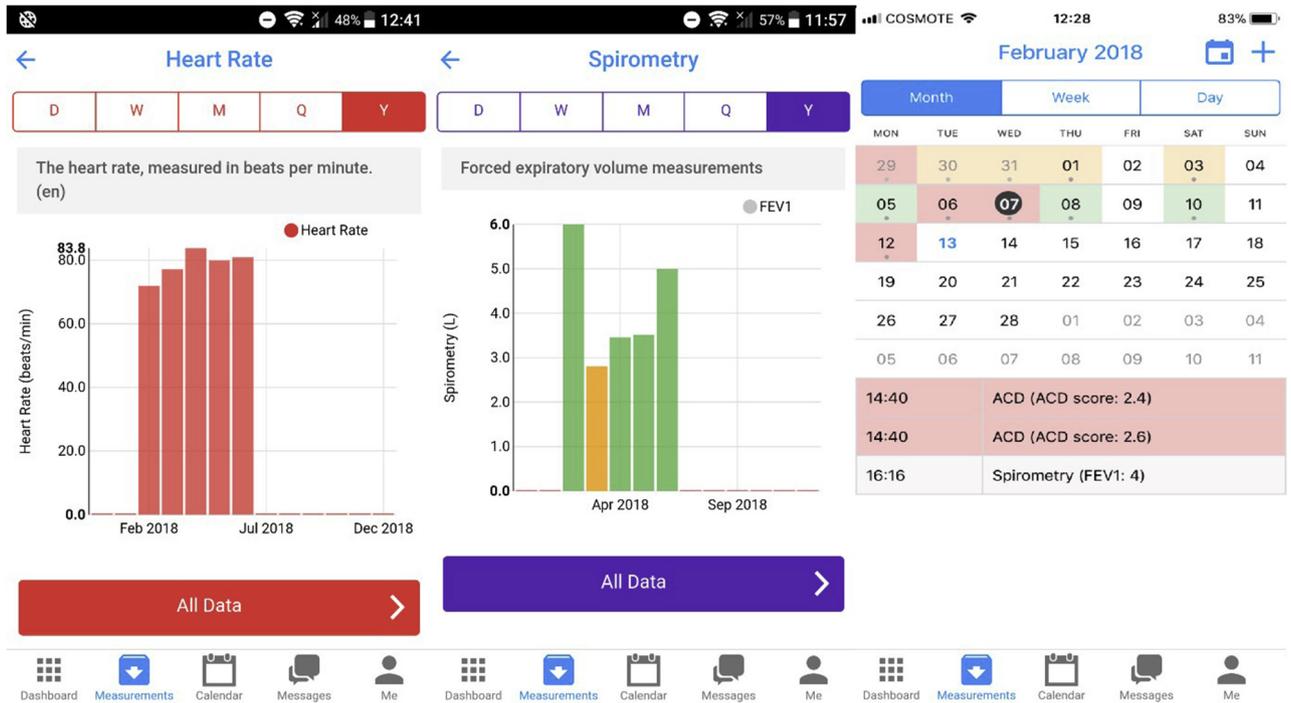


FIGURE E5. myAirCoach app: display of the gathered data. Various visualization capabilities of the collected data via the mobile app.

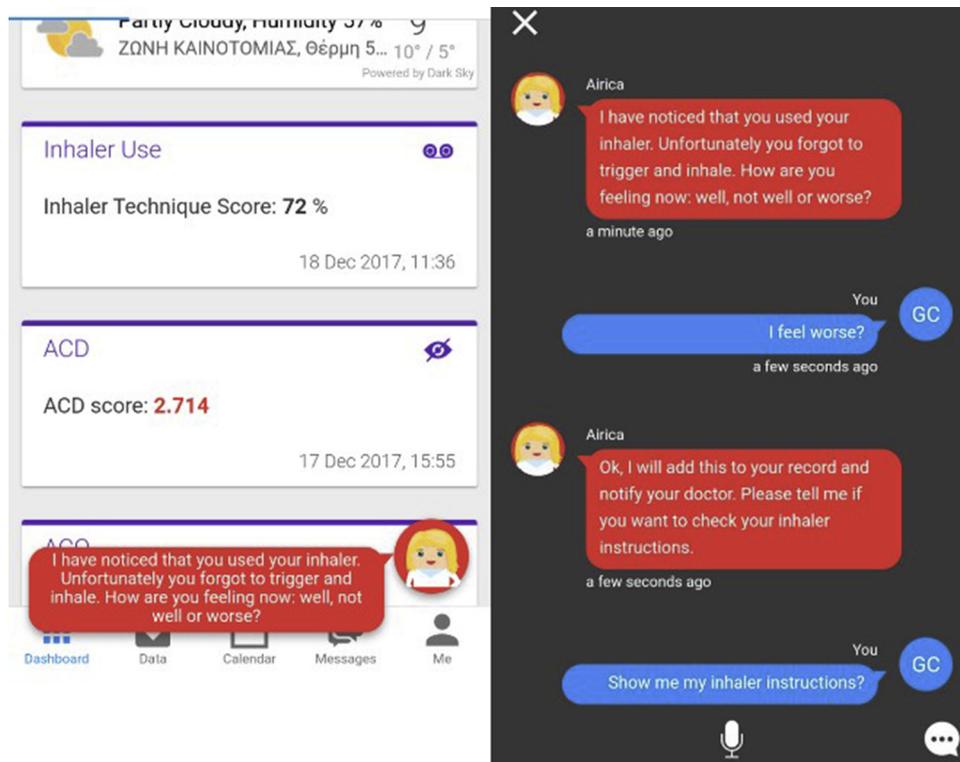


FIGURE E6. myAirCoach app: Airica. Virtual assistant based on artificial intelligence and natural language processing.

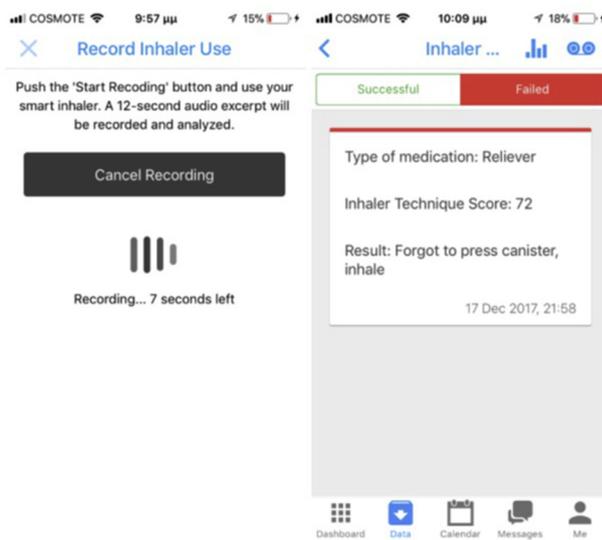


FIGURE E7. myAirCoach app: inhalation recording. Audio recording and related feedback to the participant.

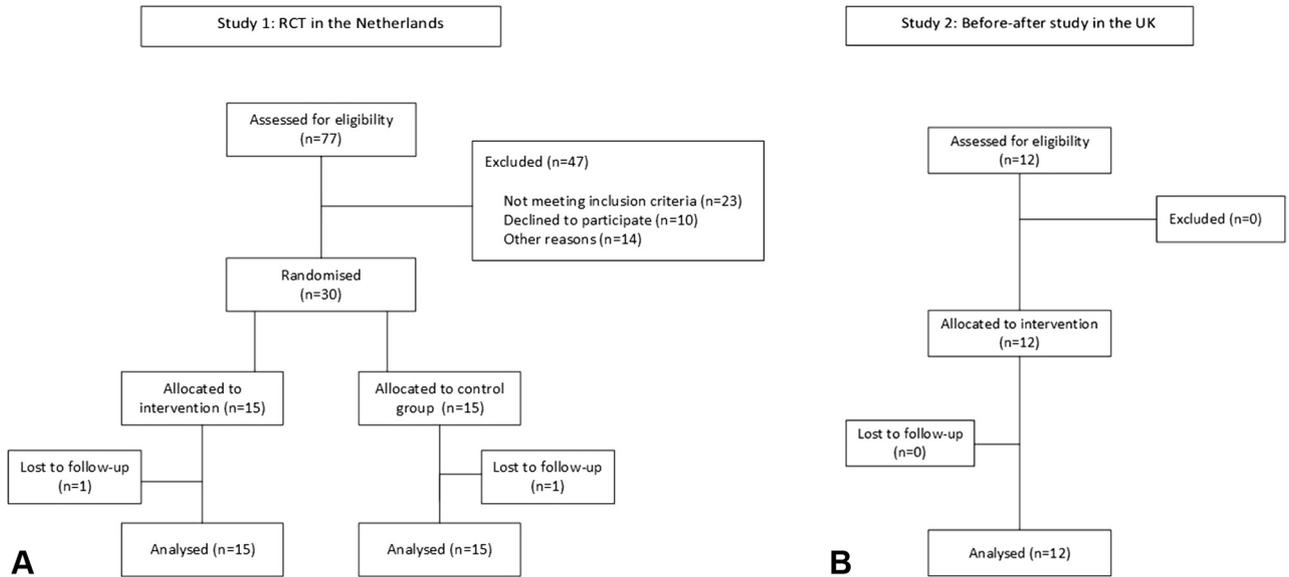


FIGURE E8. Flowchart participant enrollment. A, Study 1. B, Study 2. RCT, Randomized Control Trial.

Asthma-related Quality of Life subdomains

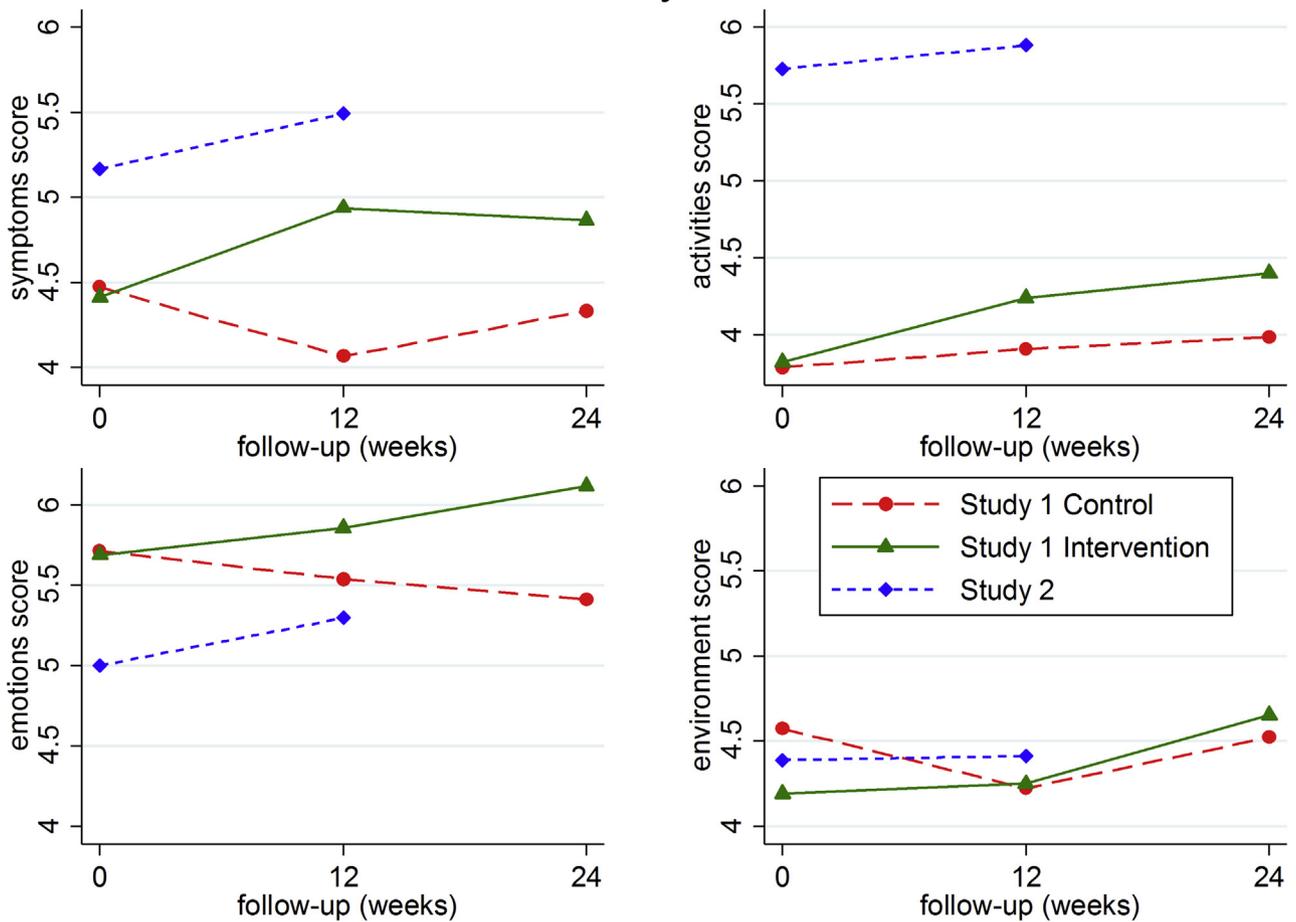


FIGURE E9. m-AQLQ domains. The m-AQLQ can be divided into 4 domains: symptoms, activity, emotions, and environment. m-AQLQ, Mini Asthma-related Quality of Life Questionnaire.

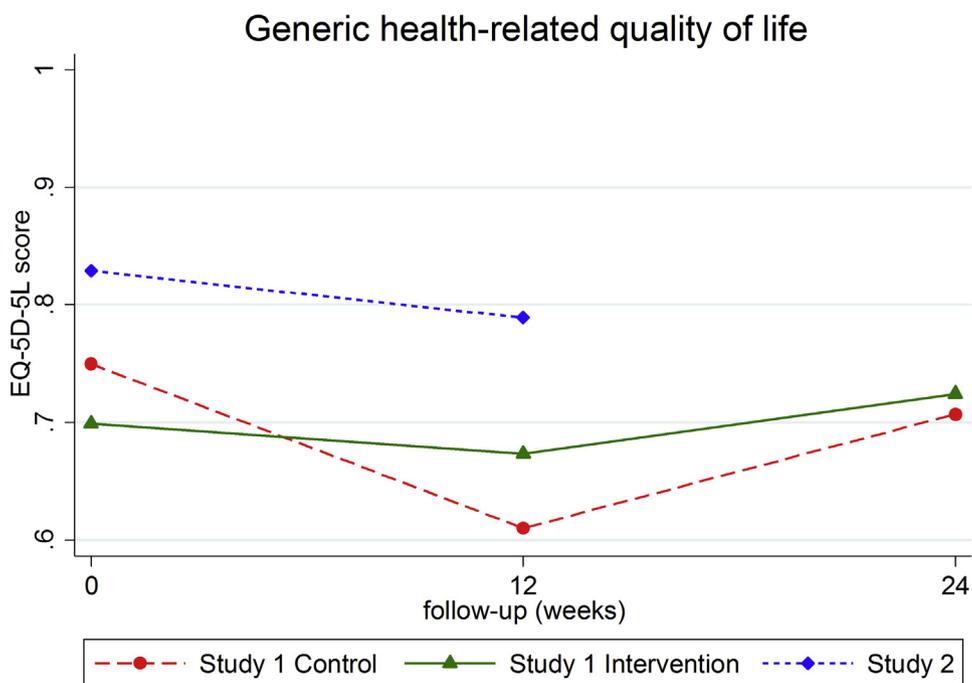


FIGURE E10. EQ-5D-5L. Generic health-related quality of life measured by the EQ-5D-5L questionnaire. *EQ-5D-5L*, EuroQol-5 Dimensions-5 Levels questionnaire.

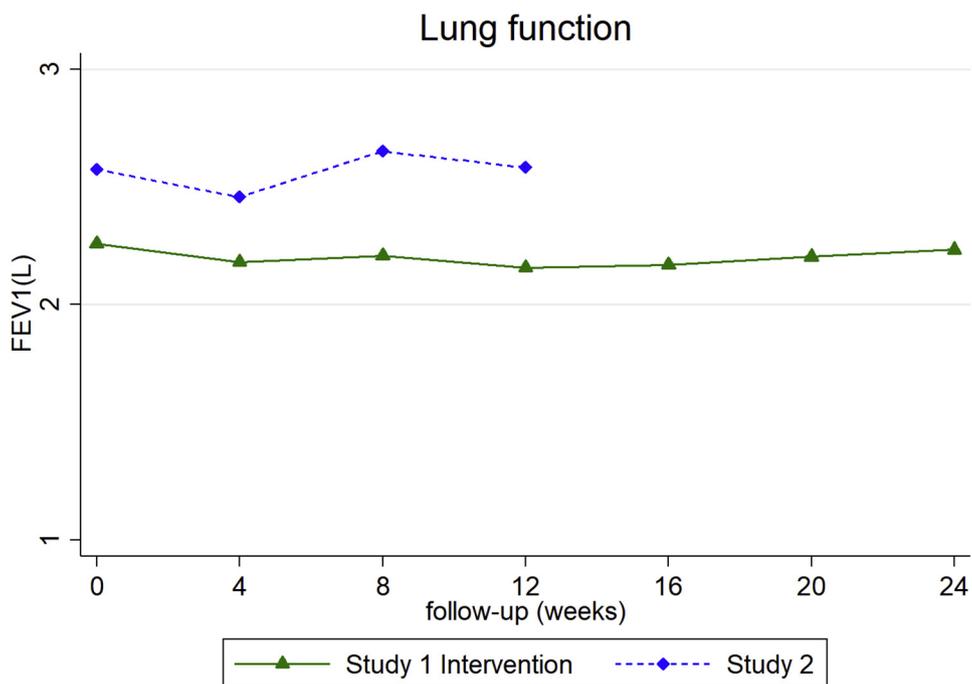


FIGURE E11. FEV1. Home-measured FEV1 by the intervention patients in study 1 and patients from study 2 with the use of the PiKO-1. *FEV1*, Forced expiratory volume in 1 second.